Remarks

Restriction Requirement

The Office alleges that the application claims five inventions. Applicants elect Group 1, claims 1-5, 7-10 and 18-19, with traverse. The Office asserts that amendments to the claims have necessitated restriction of the claims. The Office has provided no reasoning or explanation as to how clarifying amendments suggested by the Office necessitated a restriction requirement of claims that have been examined in three office actions.

A. The claims have not been amended in a manner that necessitates a restriction requirement.

The M.P.E.P. states that:

> . . . the examiner should make a proper requirement as early as possible in the prosecution, in the first action if possible, otherwise as soon as the need for a proper restriction develops. See M.P.E.P. §811.

A need for a restriction has not "developed" in this case. The amendments made to the claims on July 23, 2009 and September 11, 2009 were solely for clarity and did not alter the subject matter of the claims. That is, they still recite the same exact subject matter they did prior to the amendments of July 23, 2009 and September 11, 2009. The amendments to the claims did not change the character of the claims such that independent and distinct inventions are suddenly newly presented. These clarifying amendments did not cause a "need for a proper restriction." Therefore, no need for restriction has "developed" in this case.

The only possible legitimate reason for a restriction would be that new claims 18 and 19 recite non-elected inventions. However, as recognized by the office, these new claims do not include non-elected inventions because they have been grouped with previously existing examined claims 1-5 and 7-10 into Group I. Therefore, by the Office's admission, new claims 18 and 19 do not present new, unelected inventions.

Applicants note that the majority of the clarifying amendments were suggested to the Applicants by the Examiner in a telephonic interview that occurred on September 1, 2009. The Examiner has clearly has searched, examined and carefully considered all of the claims.

B. The claims must be examined in their entirety because no serious burden on the Office to search and examine the claims.

Two restriction requirements and **three** office actions have already been issued in this application as follows:

Restriction requirement issued June 10, 2007
Office action issued April 18, 2008
Restriction requirement issued October 24, 2008
Final office action issued February 17, 2009
Non-final office action issued April 23, 2009.

According to MPEP §803, if the search and examination of an application can be made without serious burden, the examiner must examine those claims on the merits, even though they include claims to independent or distinct inventions that would otherwise be subject to a restriction requirement. This restriction requirement has been issued after a first, second and third action on the merits. The M.P.E.P. states that:

> Before making a restriction requirement after the first action on the merits, the examiner will consider whether there will be a serious burden if restriction is not required.

See M.P.E.P. §811. There is no serious burden present in this case. In fact, the prior art for **all** of the pending claims has been searched and three Office Actions have been issued in the application. As such, there is no burden on the Office to complete a prior art search on the claims. The M.P.E.P. states that:

> If the search and examination of the entire application can be made without serious burden, the examiner **must** examine it on the merits, even though it includes claims to independent or distinct inventions.

See M.P.E.P. § 803, emphasis added. Clearly there is no serious burden in the search of the entire application because a search of all of the claims has **already been completed** by the Office. The Office has already cited alleged prior art in Office Actions, which was clearly found in a search by the Office. Therefore, there clearly is no burden on the Office, let alone a serious burden, and the Office must examine the entire application on the merits.

A restriction made after the issuance of three office action and two restriction requirements is improper because there is no serious burden to examine claims that have already been examined in three prior office actions.

Indeed, the propriety of such a restriction was recently petitioned in U.S. Pat. Appl. No. 09/478,351. There had been at least two office actions in the application prior to the issuance of a restriction requirement. The Decision dated October 31, 2008, in response to the petition states:

> Applicants' petition [sic] allege that the election requirements are improper because there would be no burden on the examiner since all of the present claims had already been rejected at least two times prior to the election requirement. For the foregoing reasons, the examiner's provisional election requirement had been deemed to be improper.

Therefore, the "serious burden" requirement precludes the finding of a serious burden where the restricted claims have been examined in at least two office actions prior to the restriction requirement. In the instant case two restriction requirements and three office actions have already been issued such that no serious burden can possibly exist to examine the pending claims.

C. Ebersole does not demonstrate the lack of a special technical feature

The Office asserts that the alleged common technical feature of the claims is the method step of adsorbing antibodies against *in vivo* expressed microbe antigens with *in vitro* microbe extracts. The Office asserts that Ebersole teaches this feature because it teaches:

> methods comprising collecting serum comprising antibodies from patients infected with *A. actinomycetemcomitans,* growing *A. actinomycetemcomitans* in culture (please note: since the bacteria is actually a single cell organism, cell culture propagation would be considered in vivo; however, in vitro could also be interpreted as "outside" a host), performing ELISAs, and performing adsorption studies. . . .

As already explained in Applicants' response of October 24, 2008, the Office's interpretation of "*in vivo*" and "*in vitro*" as used in the claims is erroneous. In the field of microbial pathogenesis, the term "*in vitro*" is used to refer to single microbial cultures grown in the laboratory and *in vivo* is used to refer to microbes that are present in the host organism. *See*, for example:

1. Hautefort & Hinton, "**Measurement of bacterial gene expression *in vivo***," Phil. Trans. R. Soc. Lond. B. (2000) 355:601 (of record), which teaches:

> The complexities of bacterial gene expression during mammalian infection cannot be addressed by *in vitro* experiments. We know that the infected host represents a complex and dynamic environment, which is modified during the infection process, presenting a variety of stimuli to which the pathogen must respond if it to be successful. The response involves hundreds of *ivi* (*in vivo*-induced) genes which have recently been identified in animal and cell culture models. *See* abstract.

2. Chiang *et al*., "***In vivo* Genetic Analysis of Bacterial Virulence**," Annu. Rev. Microbiol. (1999) 53:129 (of record), which teaches:

> *In vitro* assays contribute greatly to our understanding of bacterial pathogenesis, but they frequently cannot replicate the complex environment encountered by pathogens during infection. The information gained from such studies is therefore limited. *In vivo* models, on the other hand, can be difficult to use, and this has to some extent diminished the incentive to perform studies in living animals. However, several recently developed techniques permit *in vivo* examination of many genes simultaneously. *See* abstract.

3. Handfield & Levesque, "**Strategies for Isolation of *In Vivo* Expressed Genes from Bacteria**," FEMS Microbiol. Rev. (1999) 23:69 (of record), which teaches:

> The discovery and characterization of genes specifically induced *in vivo* upon infection and/or at a specific stage of the infection will be the next phase in studying bacterial virulence at the molecular level. . . . [*I*]*n vitro* systems initially described did not always allow the reconstruction of exact interactions between bacteria and the host. . . .[A]nimal models still represent one of the best approaches for studying *in vivo* induced (*ivi*) genes, genes defined by the process of being expressed solely *in vivo*. *See* pages 69-70.

Therefore, as evidenced by the state of the art, "*in vivo*" in not used to refer to microbes grown in single culture in the laboratory as alleged by the Office.

The Office incorrectly asserts that the common technical feature of the claims it the method step of adsorbing antibodies against *in vivo* expressed microbe antigens with *in vitro*

microbe extracts and alleges that Ebersole teaches this method step. However, one common method step of the instant claims is accurately stated as "adsorbing the antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro* and isolating unadsorbed antibodies."[1] Ebersole does not teach or suggest this common technical feature.

Finally, no undue burden exists to examine all of the herein presented claims in their entirety. In particular, the claims all contain common novel technical features including, for example, "adsorbing the antibody sample against cells or cellular extracts of the microbe or pathogen that have been grown *in vitro* and isolating unadsorbed antibodies" and "probing an expression library of clones of the microbe or pathogen with the unadsorbed antibodies."

Species Election

The Office asserts that for Group I, an election "a single specific species of what is isolated (claims 1, 18, and 19)" is required. Applicants note that claim 1 recites "a method of isolating a polynucleotide of microbe or pathogen." Claim 18 recites "a method of isolating a vaccine target for a particular microbe or pathogen" and claim 19 recites "a method of identifying a diagnostic target for a particular microbe or pathogen." Therefore, the election of "a single specific species of what is isolated" is unclear and Applicants cannot make an election because it is not clear what the different species to elected comprise. Applicants respectfully request clarification and traverse the requirement.

If the Office intended to require a species election between the 3 claims based upon their differing preambles, then Applicants note that election is improper because claims that have different preambles, but that have the same active step are not properly restricted. *See, e.g.,* Biotechnology/Chemical/Pharmaceutical USPTO Customer Partnership Meeting, June 13, 2007, Bruce Campell presentation, www.cabic.com/bcp/061307/BCampell_RBPPI_r2.ppt. Claims 1, 18 and 19 require substantially the same active steps for each of the "methods" in the preamble and are properly examined together.

[1] There are other common technical features of the claims including, for example, probing an expression library of the clones of the microbe or pathogen with the unadsorbed antibodies.

Conclusion

The third restriction requirement issued in this application is improper because The Office has not demonstrated a serious examination burden for the claims, which have already been examined and searched by the Office. The Office has recently commented on clarifying amendments to the claims in an Examiner interview. Therefore, the Office has already searched, examined, and carefully considered all of the claims. Furthermore, the amendments made to the claims on July 23, 2009, and September 11, 2008, did not necessitate a new restriction requirement because they did not change the character of the claims such that independent and distinct inventions were newly claimed. Finally, the claims do not lack a special technical feature in view of Ebersole. Applicants respectfully request withdrawal of the restriction requirement.

Respectfully submitted,

Dated: December 4, 2009 By: /Lisa M.W. Hillman/
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217-239-1962